Basic Science

Antibacterial Activity of Polyphenols from Three Extracts of *Hypericum* perforatum L.

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In recent years, the consumption of Hypericum perforatum-derived products has increased dramatically and presently it is one of the most consumed medical plants over the word. Hypericum perforatum has a wide range of medicinal applications, including skin wounds, eczema, burns, diseases of alimentary tract and physiological disorders. Beneficial propertis of H. perforatum to human health are related to the high content in phenolic compounds. Phenolic compounds are widely distributed in the plant kingdom, the content of which varies between different species and cultivars, and with maturity, season, region, and yield. Phenols play a major role in the plant. They may protect the plant against biotic or abiotic stresses, and they are also deserving for antioxidant and antimicrobial activity of plant. Phenols are classfied according to their structure as phenolic acid, flavonoids and tannins. Hypericum perforatum extracts contain many types of phenolic derivates (hypericin, hyperforin and their derivates, rutin, hyperozide, quercetin, quercitrin, isoquercitrin, caffeic and chlorogenic acid). Hypericin showed antibacterial, antiviral and anti-inflammatory activity. This study represents the antimicrobial activity of phenolic compounds from three different extracts of H. perforatum against pathogenic bacteria. The aerial parts of H. perforatum were collected in the surroundings of Kragujevac, Serbia, in July 2006 and determined in the Department of Biology, Faculty of Science in Belgrade (No.0799HP). The phenolic compounds were extracted with the following solvents: acetone, ethanol and petrol-ether. The content of total phenol (4.40-12.60 mg/g of plant), flavonoids (4.15-11.85 mg/g of plant) and non-flavonoids (0.25-1.45 mg/g of plant) in samples of the H. perforatum extracts was determined using colorimetric method, with Folin-Ciocalteu reagent. The phenolic compounds were expressed as catechin equivalents. The antimicrobial activity of plant extracts was evaluated using disc-diffusion and macro-dilution assay. The highest inhibitory effect of three extracts of H. perforatum was observed in acetone extract, which contain a high amount of phenolic compounds. The acetone extract showed the better antibacterial activity on all tested bacteria than ethanol and petrol-ether. The most sensitive bacteria was Enterobacter cloaceae. Two bacterial strains Proteus sp. and Pseudomonas aeruginosa showed resistance on all three extracts. The results obtained demonstrate a direct relationship between the phenolic content of the extracts and the antimicriobial activity.

Inventory of Medicinal Plants Used in the Amazonian Community Porvenir (Santa Cruz Department, Bolivia)

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One of the most efficient ways of finding new bioactive compounds is collecting data on the use of medicinal plants in unexploited areas. The Baio Paraguá Indian Reservation in the Bolivian Amazon is a highly valuable source of medicinal plants because of the importance of traditional medicine, but it has not been studied thoroughly. Porvenir, with 550 inhabitants, is one of the four communities of the Reservation, which is populated by Mestizos and indigenous people, including the latest Guarasug'we Indians. Ethnobotanical and ethnomedical data (common names, habits, parts of the plants used, preparations, illnesses treated) were recorded for the plants used by at least 10% of the adult inhabitants. During the 5-month long field work techniques of cultural anthropology (participating observation, semi-structured interviews) were applied. The traditionally used medicinal plants were collected and botanically identified, and voucher specimens were deposited in the National Herbarium of the Noel Kempff Mercado Natural History Museum. The knowledge on medicinal plants were analyzed by means of A. H. Gentry's method which gives the frequency and variety of the use of plants. The data collected from the inhabitants of Porvenir were compared with data collected from the people of other countries and traditional communities and with the results found

in the chemical, pharmacological and clinical literature. The traditional use of herbs was evaluated whether it correlates with the relating scientific data. A total of 235 plants were listed and among them 135 species were used in the traditional phytotherapy. A total of 345 medicinal uses for the healing of 97 different illnesses were obtained. Large proportions of medicinal plants were recorded to have been used for the treatment of gastro-intestinal complaints (40%), respiratory (24%), dermatological (22%), urinary (17%), parasitic (17%), gynecological (15%) and hepatobiliary (14%) diseases. The traditional use of the plants is supported by pharmacological data only in case of 35% of the species and neither chemical nor pharmacological data on 20% of the species were found in the literature. It was concluded that there are no or only few studies available on the chemistry and pharmacology of the most plants used by people from Porvenir. These species offer a good subject of investigation to find new biologically active compounds.

Chemical Composition of Essential Oil from *Juniperus communis* L. and Influence on Growth and Metabolism of Certain Bacteria O. Stafanovic, D. Stanoiavic, L. J. Comic, M. Matovic and S. Curcio.

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The antimicrobial properties of essential oils have been investigated for many years and their preparations have found applications as natural antimicrobial agents in the field of pharmacology, pharmaceutical botany, phytopathology, medicinal and clinical microbiology and food preservation. Previous investigations established that essential oil of Juniperus communis L. (fam. Cupressaceae) have significant antifungal and antibacterial properties. Whereas the synthesis of biotically active substances in plants is in large measure dictated by climato-geographical factors, the aim of this work was to identify chemical composition of essential oil of species J. communis L. that grows wild in Serbia. Also, the purpose of the present work was to detect changes in growth and metabolism of certain bacterial species arising in the presence of essential oil in vitro. The essential oil of the dry, ground fruits of J. communis L. was obtained by hydro-distillation in a Clevenger apparatus. The components of the essential oil were indentified by gas chromatography-mass spectrometry (GC-MS) analysis. The influence of essential oil of J. communis L. on growth and metabolism of bacteria was monitored from changes of population density and total protein content. The changes of population density were determined spectrophotometrically at 575 nm; total protein content was determined by Lowry method. The following species of bacteria were used in the investigation: Agrobacterium tumefaciens, Bacillus subtilis, Escherichia coli and Pseudomonas fluorescens. The essential oil analysis resulted in the identification of 32 constituents. The major constituents of oil were: α -pinene (30.763%), sabinene (19.372%), β-myrcene (16.427%), epi-bicyclosesquiphellandrene (6.376%), I-limonene (4.906%). It was established that essential oil of J. communis L. affect growth and metabolism of tested bacteria. The intensity of action varied depending on the species of micro-organism The least changes were recorded in growth and metabolism of E. coli. In conclusion, this study shows that essential oil of J. communis L. possess significant antibacterial activity in vitro, that can be attributed to the presence of various substances, mainly the phenolic monoterpene. Further studies will be necessary to investigate the effect of essential oil of J. communis L. against other bacterial species.

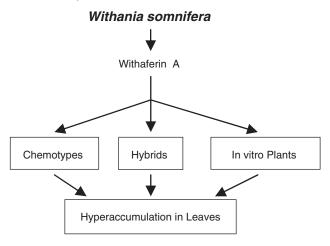
Production Dynamics of Withaferin A—A Potential Anticancer Withanolide in Different Chemotypes, Hybrids and *in vitro* Propagated plants of *Withania somnifera* complex

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Withania somnifera popularly known as Ashwagandha, is an important drug of Indian Traditional Medicine used in 114 standard herbal preparations. Withaferin A is an important withanolide holding promise in cancer treatment and relatively safe radiosensitive/chemotherapeutic agent. It is present in traces in all parts of W. somnifera excepting leaves, whereas it is reported to be present in only two non-Indian chemotypes (South African chemotype/Israel chemotype 1).

The present studies have marked its presence in all Indian populations (wild/cultivated) as well as two identified Indian chemotypes (AGB002 and AGB025). The quantitative dynamics of Withaferin A production in Indian populations and interchemotypic hybrids developed at our institute have been studied and the results were compared with earlier reported five chemotypes from Israel, South Africa and India. An analysis on inheritance characteristics based on presence/absence of Withaferin A in hybrid plants and their respective parents is given for future studies on the chemogenetics of this complex species in greater details. Further, production potential of Withaferin A in *in vitro* propagated plants of elite varieties developed at this institute is discussed in view of maintaining chemotypic fidelity and stability from production point of view. Besides, it is seen that *in vitro* rapid amplification and chemical homogeneity of a designated genotype or a hybrid line for pilot production of this bioactive compound could be achieved. Also evidence-based clue suggesting leaf as the site of synthesis of Withaferin A is provided.



Leaves > Fruiting Calyx > Stem > Berries > Root > seed

Lisosan G, a powder of grain, decreases the oxidative stress produced by carbon tetrachloride in rat liver

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Lisosan G is powder of grain registered to the Italian Minister of Health as alimentary integrator. In this investigation, the effects of Lisosan G on the drug metabolizing system, its antioxidative property and its hepatoprotective efficacy against carbon tetrachloride-induced liver toxicity in rats was studied. The treatment of rats for 4 days with 0.5 g/kg of Lisosan G had no effect on various drug metabolizing enzymes as determined with the marker substrates for the cytochrome P450 1A, 2A, 2B, 2E1, 3A and glutathione s-transferase, NAD(P)H: quinoneoxidoreductase and UDP-glucuronosyl transferase activities. Experiments in vitro showed that Lisosan G had radical scavenger activity. A confirmation of the antioxidative property of Lisosan G was also confirmed when it was administered in vivo to carbon-tetrachloride-intoxicated rats. The increased alanine aminotransferase, aspartate aminotransferase, lipid peroxidation activities and the decreased glutathione content observed in the carbontetrachloride- treated rats were restored to the control rat levels when the rats were previously treated by gavage with 0.5 g/kg of Lisosan G for 4 days before carbon-tetrachloride injection. In conclusion, the results showed that Lisosan G did not interfere with cytochrome P450 and phase 2 enzymes, had antioxidative properties and protective effects versus the carbon-tetrachloride-induced hepatotoxicity.

New Flavonoids from Butanol Extract of Launaea arborescens

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Phytochemistry investigation of the butanol fraction of water-acetone extract of aerial part of *Launaea arboescens* led to the isolation of seven flavonoids and other polyphenols. The structures of these compounds were identified

as 4',5'-di-methoxy 7-(5"-me hexan)1-oyl flavanone 1, 5,4',5'-tri-hydroxy 7-(3"-me butan) -yl flavanone 2, 3"-isopropyl pyrano [1":7, 4":6] 3',4',5', 5-tetrahydroxy flavanone 3, 7-O-[α -rhamnopyranosyl-(1->6)- β -glucopyranosyl] 4', 5, 7-tri-hydroxy-flavanone 4, 7-O-[α -rhamnopyranosyl-(1->6)- β -glucopyranosyl] 3',5-dihydroxy 4'-methoxy flavanone 5, 7-O-[α -rhamnopyranosyl 4',5, 6-Trihydroxy flavone 6, 5,6,7,4'-tetrahydroxy flavonol 7, using spectroscopic analysis.

Photochemical Screening of *Dioscorea* species for Biological Activities Bharati S. Meti

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Dioscorea is one of the economical important genuses of Dioscoreacea showing multipurpose benefits. Three species of the Dioscorea have been tested for antimicrobial (against four bacteria & two fungi), anti-inflammatory, antianalgesic and anticonvulsive activities. Dioscorea plant extracts have shown antibacterial activity against Escherichia coli, Pseudomonas aereugenosa, Proteus vulgaris and the antifungal activity for (Candida albicans and Cladosporium cladosporoides). Chloroform and distilled water extracts of D. intermedia have shown antibacterial activity only against P. aeruginosa and anti-inflammatory activity has been observed in all three species. Dioscorea pentaphylla has shown significant inhibition (61:76) of paw edema compared to diclofenac sodium (64:70) when used as standard. Dioscorea interemedia and D. alata have also shown anti-inflammatory activity. Analgesic and anticonvulsive activity has been observed in all the three species.

15R-16,17-Seco-subincanadine E, a Proerectile Indole Alkaloid Isolated from Aspidosperma ulei Stem Bark

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The search of an effective, safe and easy to administer drug for use in erectile dysfunction, impotence and fertility has been a perennial pursuit of most societies from times immemorial to throughout the history. Plants that belong to the genus Aspidosperma (Apocynaceae) are known to be very rich in indole alkaloids and have an ethnomedical history of use as traditional remedies for erectile dysfunction. In the search for novel drugs effective against erectile dysfunction, this study examined whether the indole alkaloid 15R-16,17-secosubincanadine E (SEC) isolated from Aspidosperma ulei Markgr. stem bark could manifest penile erection-related behavioral responses (penile erection, erection-like and genital grooming) in mice. In the method described by Rampin, intraperitoneal injection of SEC (12.5; 25 and 50 mg/kg) elicited all the three different behavioral responses in a manner similar to yohimbine (YOH 2 mg/kg), a known indole alkaloid. Seventy-five percent of mice treated with SEC (P<0.001 versus control) showed penile erections, which were completely blocked by clonidine (P<0.001 versus SEC), ana α -2-adrenoceptor agonist and haloperidol (P<0.001 versus SEC), a dopaminergic antagonist and as well as by L-NAME (P<0.05 versus control), a nitric oxide synthase inhibitor. In conclusion, the data obtained in this study clearly demonstrate that SEC facilitates penile erection in mice possible through the activation of central dopamine and blockade of presynaptic α -2 adrenoceptors with a subsequent enhancement of nitric oxide release from the penile nerves and arteries. This study further supports the traditional use of extracts from Aspidosperma species in erectile dysfunction.

Studies in Hepatocyte Activity and the Structure Relationships and Luteolin Derivatives from *Chrysanthemum fuscatum*

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In order to evaluate the protective effect of the isolated compounds from Chrysanthemum fuscatum in carbon tetrachloride rat-induced cytoxicity, primary cultured rat hepatocytes have been adopted as a screening system. The flavonoid glycosides isolated from $\it C.~fuscatum$ exhibited a protective effect by different mechanisms. Luteoline-O-7 glycosyl (50–300 μ M) inhibited indices of cell damage (LDH leakage TBARS production and GSH depletion), in a dosedependent manner Quercetin-O-3 glycosyl, 7 methoxyl, in particular, exhibited a stronger cytoprotective activity by inhibiting CYP2E1 activity in the intoxicated hepatocyte.

Antioxidant Defense System in Experimental Hyperthyroidism: Effects of Trigonella foenum-graecum (L) Papilionaceae

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Trigonella foenum graecum seeds (TGS) is a traditional plant is several diseases. Free radical-mediated oxidative stress has been implicated in the genesis and exacerbation of degenerative diseases. In view of the role of oxidative process in thyroid disorders, in this study, we investigated the antioxidant status of erythrocyte lysates in experimental hyperthyroidism induced by I-thyroxine and ethanolic extract of (TGS) at a dose 300 mg/kg body weight supplementation on defense systems. Our findings of significantly increased T4, T3 and TSH values in thyroxine-administered rats confirmed the establishment of hyperthyroidism. Superoxide dismutase (SOD), glutathione peroxidase (SOD), glutathione peroxidase (GSH-Px) and glutathione GSH) values found to be significantly increased in hyperthyroid rats in comparison to control group. TGS supplementation to hyperthyroid rats induced a significant decrease in antioxidant parameters. Our results show that hyperthyroidism increases the components of antioxidant defense system in erythrocyte lysates. Furthermore, TGS supplementation reduces the oxidative stress in hyperthyroidism rats.

Hypoglycemic Activity of Algerian Medicinal Plant Ajuga iva (L) Schreb, Labiatae (Lamiaceae): Antioxidant Status and Effect on Lipid Peroxidation in Streptozotocin Rats

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Ajuga iva is widely used in Algerian folk medicine for the treatment of diabetes mellitus. However, very few scientific and medical studies were carried out on the efficacy and toxicity of A. iva. In this study, we report the hypoglycemic butanolic extracs of A. iva in normal and streptozotocin-induced type I diabetic rats. Oral administration of 10 mg/kg body weight (A.E) of aqueous extract/and 100 mg/kg body weight (B.E) of butanolic extract of A. iva for 3 weeks resulted in a significant reduction in blood glucose and an increase in total hemoglobin. The extracts prevent decrease in body weight and also resulted in decrease of free radical formation in liver tissue. This study shows that both A.E and B.E of A. iva have an antihyperglycemic action. The decrease in thiobarbituric reactive substances (TBARs) and increase in reduced glutathione (GSH), glutathione peroxidase (GSH-Px), mitochondrial superoxide dismutase (Mn-SOD), cytosolic superoxide dismutase (Cu-Zn SOD) and catalase (CAT) clearly shows the antioxidant property of A.E and B.E of A. iva. Our data indicated that A. iva extracts are able to ameliorate oxidative damages induced STZ diabetic rats and it may be a candidate for development as an antidiabetic agent in humans.

The Signature of the Plants: Its Role in Ancient and Modern Medicine Matonti Loredana

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The Doctrine of Signatures is a mixture of philosophy and medical theory and was expounded by a variety of people, from chemists to philosophers, alchemists to medical practitioners. The appearance of the Doctrine of Signatures (Doctrine of Correspondences) in tradition cuts across cultural boundaries. Nature-based cultures from all over the world believe in the interconnectedness of all things. Evidence of the application of this tradition appears in European, Native American and Oriental history. Further support may be found in rich allusions in mythology. The theory states that many things of God's creation (plants, animals, minerals, etc.) hold a clue to their usefulness in their external characteristics. It is an old tradition, or a part of many traditions, that plants (as well as animals and minerals perhaps) have clues or 'signatures' in their shapes and forms and actions and things that tell what their purposes are. When specifically applied to medicinal plants, the DOS claims that a plant's medicinal value can be determined by observing the various characteristics and habits of the plant (signatures); mode and location of growth, shape of leaves, color of flowers. By symbolic association, a plant's appearance is linked to the disease that it can be used to treat. Many of the common names for plants (eyebright, toothwort, bloodroot) suggest their use according to the DOS. It is widely known that through the Doctrine of Signatures is how we got, for example, aspirin and the heart medicine digitalis. Dismissed as superstition at the turn of this century as 'Heroic' medicine replaced the earlier, long-standing traditions of natural medicines, the Doctrine of Signatures has been unrightfully dismissed without being subjected to the empirical processes of science, whereby experimentation is applied to verifying or disproving a particular proposition, and probably a lot of research seems to be confirming this rather than disproving it Researching substances in laboratories is a modern way of trying to understand the universe. The various components of a subject are taken apart, isolated and carefully studied. This is contrary to the past where people would observe a complete plant, animal or mineral in its natural surroundings, to gain information on its characteristics. These traditions already employing the Doctrine of Signatures have made inestimable contributions to medicine, and continue to do so. Each shape has a corresponding frequency. The shape is not a coincidence because it is an expression of the frequency through which the form is evident to us. Each substance has got a personal vibration, like a personal fingerprint, Paracelso called it 'signatura rerum'. An innovative science such as quantum physics perhaps will give us the key to interpret this in the future. The beauty of the Doctrine of Signatures lies in the fact that it provides insight into the archetypes that manifest within and out of the Universe and help one understand the processes by which they are woven into life.

Anti-trypanosoma Activity of Some Medicinal PlantsA. R. Gohari¹, S. Saeidnia¹, T. Yagura², M. Ito¹ and A. Hadjiakhoondi¹ ¹Medicinal Plants Research Center, Faculty of Pharmacy, Medical Sciences/University of Tehran, Tehran, Iran and ²Department of Pharmacognosy, Graduate school of Pharmaceutical sciences, Kyoto University, Kyoto, Japan

Some of the medicinal plants are a potential source of new drugs to improve the treatment of Chagase disease whose treatment is still a challenge. Previously, we reported the effect of some Satureja, Dracocephalum and Achillea species against the epimastigotes of Trypanosoma cruzi which lead to isolation and identification of the active components. Here in this screening, the in vitro trypanocidal activity of some fractions for 17 medicinal plants, collected from the northern part of Iran, has been reported. Aerial parts of the plants were dried carefully and reduced to small pieces, followed by extraction with hexane and methanol, successively, by maceration at room temperature. Then the solvents evaporated under reduced pressure to obtain the concentrated extracts and dried under vacuum in order to give dried powder of extracts. Different concentrations of the plant extracts in ethanol were investigated against the epimastigotes of T. cruzi. The movement of epimastigotes was observed under a microscope. We assumed that immobilized organisms were died. The negative control contained ethanol in the same proportion utilized to dissolve the drugs. Each assay was performed in duplicate together with gentian violet as a positive control with MLC= $6.3\,\mu M$. Using hexane extracts of Rubus hyrcanus and Salvia sclerae the most of the activity against epimastigotes of $T.\ cruzi\ (MLC=12.5\,\mu M)$ has been observed. Hexane fraction of Marrubium vulgare was active with MLC=25 μM. Among the methanol extracts of the plants, S. sclerae was the only effective one (MLC=50 μ M). Echium amoenum, Satureja macrantha, S. atropatana and Stachys laxa did not show activity lower than 100 µM in both hexane and methanol extracts. Some of the Iranian medicinal plants (S. sclerae, M. vulgare and R. hyrcanus) could be the promising source of active components against the epimastigotes of T. cruzi and need to further phytochemical and pharmacological studies.

A Contribution about the Essential Oil of Artemisia sieberi in Iran

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The genus Artemisia is one of the largest and most widely distributed of the nearly 100 genera in the tribe Anthemideae of the Asteraceae (Compositae). Several secondary metabolites characterize the chemical composition of the genus Artemisia. A survey of the literature indicates that almost all classes of compounds are present in the genus, with particular reference to terpenoids and flavonoids. The wide array of molecules present in the genus and the distribution of plants in several different habitats provide the opportunity for the study of genotypic and phenotypic variations as well as chemotaxonomic relationships among species. The terpenoids present in Artemisia species are representative of all classes of compounds, from monoterpenes up

to triterpenes. Most of the species are characterized by the typical fragrance of lower terpenoids, such as monoterpenes and sesquiterpenes. These volatile molecules are present in the essential oils, which impart important strong aromatic odors to the plants. Among the various compounds, lower terpenoids such as camphor, thuione, borneol and 1.8-cineole are the most representative. As for many aromatic plants, the oil content of Artemisia is affected by environmental factors. Thirty-four species of Artemisia has been reported in Iran. Artemisia sieberi is the most distributed in Iran. In this research, yield and chemical composition of the essential oil of A. sieberi are studied in 34 habitats of Iran. Aerial parts of nature and farm plants were collected at full flowering stage. The exact date and place of each harvesting have been. The collected plants were dried at room temperature and after 48 h hydrodistilled for their essential oil. The herbarium specimens have been deposited in the herbarium of Research Institute of Forests and Rangelands (TARI). Also seeds of each habitat were collected and planted in homogeneity condition of farm. They are hydro-distilled as well as natural plants. The essential oils of all harvested plants (nature and farm) were isolated by hydro-distillation in Clevenger-type apparatus for 3.5 h. The oils were dried over anhydrous calcium chloride and stored in sealed vials at low temperature before analysis. Yields of essential oils isolated from the aerial parts of A. sieberi at full flowering stage have been shown. The components of oils were identified by comparison of their mass spectra with those of a computer library or with authentic compounds and confirmed by comparison of their retention indices either with those of authentic compounds or with data published in the literature. Yield of essential oil in most natural habitats are higher than the farm. It can be because of drought stress in natural habitats (the farm irrigated regularly). Mean of essential oil yields in nature and farm were compared by Student's t-test: P=0.001, yields in nature and farm had significant difference at 99.9% level. In this research, we studied regression relationship between yield of essential oil in natural habitats with climate, altitude and soil characteristics. Their effects were not significant. Total of common chemical components in nature and farm plants were analyzed by Student's t-test. They have equal variances (Levin's test) and normal distribution (Anderson-Darling Normality test). P>0.05: NS (non-significant) P<0.05: *(significant at 95%) P<0.01:**(significant at 99%) P<0.001: ***(significant at 99.9%). Camphene, 1,8-Cineole, β-thujone, camphor, borneol, did not have significant difference. But (z)-β-ocimene and chrysanthemyl acetate at 95% level, p-cymene, α -thujone, pinocarvone, terpinen-4-ol at 99% level, (E)- β - ocimene, γ -terpinene, myrtenol and bornyl acetate at 99.9% level had significant difference. Therefore, non-significant components are influenced by environmental factors lower than significant components. Main chemical components were camphor, 1,8-cineole, α -thujone, β -thujone and camphene. Most of these components did not have significant difference between nature and farm or they did not get affected by environmental factors.

New Directions in MANUAL Therapy: Matrix Extracellular and Fascia—Regulation and Deregulation in Depth

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The fascia is a connecting tissue that pervades the entire organism covering all of its surface and depth. Anatomists clearly understand this structure and that it is actually a constant continuum inside the organism. Although the fascia is in strata ranging from superficial, to medium and to deep, during an anatomic dissection it is possible to understand the continuity that exists within muscles, ligaments, bones, vase, nerves and organs. In fact, these are kept together by this large network of collagen fibers and reticulates that clasp all without a solution of continuity. Besides this connecting role, the fascia plays a role in many other functions, such as circulation and immunization, including the mechanic function at cellular, tissular and articular level. The fascia is substantially made up of a matrix, which is water, glycoprotein and mineral salts, where molecules of adhesion like integrins and caderines swim, with specialized cells like fibroblasts, free cells like the macrofages, the lymphocytes and the monocytes and fibers of collagen, reticulate and elastic that are a products of the regulation function of the fibroblast. Because of its anatomic and histologic characteristics, this tissue—unknown and not really taken into consideration for functions that go beyond that of coating-seems to draw a growing interest, in particular for its constant participation in the regulation activity of the extracellular matrix. From a phylogenetic and ontogenetic point of view, the fascia represents the first system of cellular communication and it is right here that we find the first regulatory answers that every organism activates when stimulated in whatever way. From recent studies carried out in molecular biology, it would seem that mechanical stimulations have a regulatory effect both on the extracellular matrix and on the cells, modifying not only physical conditions like the density or the viscosity of the liquid component, but also processes, like cellular mobility, angiogenesis, inflammation or immunity reactions. This recent information opens up new paths and new reflections on the usage of the forces applicated in manual therapy, thus developing new therapeutic models. Moreover, evidence that the action of the mechanical force activates regulation answers of the vegetative system or Grundsystem, named by Pischinger, opens up the therapeutical potential of manual therapy, often only used to intervene exclusively on scheletal muscle problems and not enough in other pathologies.